Chem. Soc., **6**, 241 (1985).
5. C. Lee, O.C. Kwun and H.T. Kang, *ibid.*, **7**, 73 (1986).
6. J. Arunachalam and S. Gangadharan, *Anal. Chim. Acta*, **157**, 245 (1984).
7. J. Arunachalam and S. Gangadharan, *J. Indian Acad. Forensic Sci.*, **20**, 54(1981).
8. D. Coomans and D.L. Massart, *Anal. Chim. Acta*, **112**, 97 (1979).
9. C. Lee, O.C. Kwun, S. Kim, I.C. Lee and N.B. Kim, *Bull. Korean Chem. Soc.*, **7**, 347 (1986).

The Synthesis of *p*-acetylcalix[4]arene via Fries Rearrangement Route

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Starting with the readily available *p-tert*-butyl-calix[4]arene 2, *tert*-butyl groups are removed by $AlCl_3$-catalyzed de-alkylation reaction, and the calix[4]arene 3 formed is converted to the tetraacetate 4. This compound undergoes Fries rearrangement to yield *p*-acetylcalix[4]arene 6, which seems to be an attractive starting material for the introduction of functional groups. As a preliminary experiment *p*-(1-hydroxyethyl)calix[4]arene 7 is prepared by $LiAlH_4$ reduction of 6.

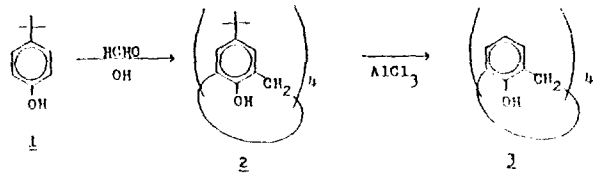
Introduction

Calixarenes which have various functional groups are attractive with respect to the long term goal of calixarene research, *viz.* the construction of enzyme models. *p-tert*-Butylcalix[4]arene 2 has become one of the most accessible of all the known macrocyclic cavity-containing compounds, obtainable in the yield[1,2] greater than 50% from the base induced condensation of *p*-butylphenol and formaldehyde. $AlCl_3$-catalyzed de-*tert*-butylation has been shown to proceed in excellent yield,[3] making calixarene 3 an extremely attractive starting material for the preparation of various para-functionalized calix[4]arenes.

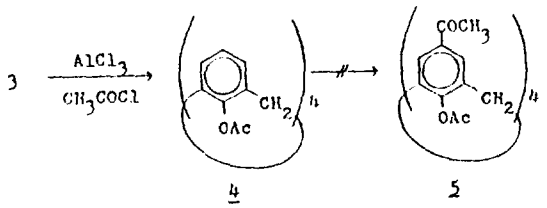
Direct introduction of functional groups into the calixarene via electrophilic substitution has been attempted in several laboratories, however, failed in most cases. The limited successes that have been published are the sulfonation of calix[6]arene by Shinkai and coworkers,[4] the bromination of calix[4]arene by Gutsche and coworkers,[5] and the nitration of calix[4]arene in our laboratories.[2]

Due to the carbonyl group can be converted to various functional groups by several ways such as oxidation, reduction, Grignard reaction and Wittig reaction, we repetitiously attempted to introduce carbonyl function into the para positions of calix[4]arene 3 *via* Friedel-Crafts acylation reaction and Reimer-Tieman reaction. To our disappointment, however, all the attempts failed. Friedel-Crafts conditions resulted in O-acylation rather than *para*-acylation, and the resulting esters failed to undergo further reaction at the para positions. Gutsche and coworkers also reported the same results.[6]

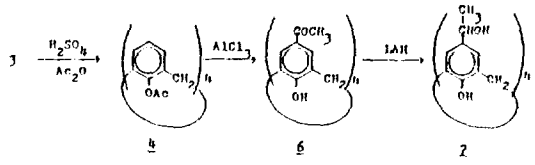
When calix[4]arene 3 was treated with Reimer-Tieman condition, only unidentified products were resulted without any indication of introduction of aldehyde groups into the para positions of calix[4]arene. Recently Gutsche and coworker[6] reported the preparation of the methyl ether of *p*-carboxycalix[4]arene starting from *p*-bromocalix[4]arene obtained by bromination of the calix[4]arene followed by lithiation and carbonation. In the similar fashion, they prepared the methyl ether of *p*-acetylcalix[4]arene by Friedel-Craft acylation of the methyl ether of calix[4]arene.



Scheme 1



Scheme 2



Scheme 3

As an alternate route for the introduction of carbonyl functions into the para positions we explored the Fries rearrangement route. In Fries rearrangement,[7] phenol esters rearrange in the presence of metal halide catalysts to form *ortho*- or *para*-hydroxy ketons depending upon steric and temperature factors. Since all the ortho positions in calix[4]arene are oc-

cupied by the methylene bridges, *para*-isomer would be the expected product of rearrangement, Fries rearrangement seems to furnish a useful method for converting calix[4]arene tetraacetate 4 to *p*-acetylcalix[4]arene 6. Here we report the preparation of *p*-acetylcalix[4]arene as shown on scheme 3.

Gutsche and coworkers prepared the tetraacetate of calix[4]arene 4 in 53% yield by treatment of calix[4]arene 3 with Ac_2O and *p*-toluenesulfonic acid as catalyst. In this investigation we prepared compound 4 in 75% yield by treatment of compound 3 with Ac_2O and H_2SO_4 as catalyst, following general procedures for the acetylation of calixarenes.[9]

At an early stage of present work, the rearrangement reaction was attempted with solvent such as CS_2, ethylene dichloride and nitrobenzene, without any indication of product formation. When a mixture of 4 and $AlCl_3$ was heated, the product was found to be a mixture of starting material 4 and the desired product 6. Experiments with various reaction times and temperatures showed the optimum reaction conditions to be 18h at 150°C. Shorter reaction time and low temperature decreased the rearrangement reaction, and longer reaction time and higher temperature increased the complexity of the reaction product mixture and increased the difficulty in the purification of the desired product. Initially, we tried to isolate the desired product 6 by recrystallization from various solvents and solvent mixtures. However, sometimes worse product was obtained from recrystallization. It was then observed that there is a big difference in the solubility of these two compounds in benzene; the starting compound 4 is soluble in boiling benzene, but the desired product 6 is only slightly soluble in boiling benzene. Thus, compound 6 could be isolated by this solubility difference in benzene. The reaction product mixture was boiled with benzene. The insoluble material was collected and then treated with cold acetone to obtained pure *p*-acetylcalix[4]arene 6 in 64% yield. The ^{1}H-nmr and IR characteristics of 6 are commensurated with the assigned structure. The compound 6 shows very limited solubility in various common solvlents including acetone, chloroform, benzene and THF which also supports the calixarene structure as suggested by Zinke.

As mentioned earlier in this paper, *p*-acetylcalix[4]arene seems to provide an attractive starting material for the preparation of calixarenes which contain various functional groups on *para* positions. As a preliminary experiment to explore these possibilities, the reduction reaction was investigated. When a THF solution of 6 was treated with $LiAlH_4$ at room temperature *p*-(1-hydroxyethyl)calix[4]arene 7 was obtained in 71% yield. The assigned structure was supported by its ^{1}H-nmr and IR characteristics.

The preparations of various *para*-functionalized calix[4]-arenes using the *p*-acetylcalix[4]arene as starting material are now under investigation in our laboratories and the results will be published soon.

Experimental

IR spectra were obtained by using a Perkin-Elmer 170B spectrophotometer and ^{1}H-nmr spectra were recorded on Varian EM 360A instrument, with TMS as internal standard.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrahydroxy-calix[4]arene 2 was obtained in 52% yield by base-induced condensation reaction of *p*-*tert*-butylphenol and formaldehyde as described elsewhere;[2] mp 344-346°C (lit[9] 344-346°C).

25,26,27,28-Tetrahydroxycalix[4]arene 3 was obtained in 74% yield by $AlCl_3$-catalyzed removal of the *tert*-butyl groups from *p*-*tert*-butylcalix[4]arene following the published procedures;[2] mp 315-317°C (lit[3] 314-318°C).

25,26,27,28-Tetraacetoxycalix[4]arene 4. 3.00g (7.07 mmole) of 3 was treated with 64m*l* of acetic anhydride and 2 drops of conc. H_2SO_4 The mixture was heated under reflux for 1.5h and poured into 300m*l* of ice-water, and the precipitate was separated by filtration to yield 4.56g of grey colored solid. Two times recrystallization from benezene gave 3.15g (75%) of colorless crystalline solid; mp 395-397°C (dec) (lit[8] 399-402°C dec); IR(KBr) 1735 cm^{-1}(C=O stretching); ^{1}H-nmr ($CDCl_3$) δ 7.10 (s, 12, ArH), 3.75 (s, 8, CH_2), 1.55 (s, 12, CH_3).

5,11,17,23-Tetraacetyl-25,26,27,28-tetrahydroxycalix [4] arene 6. A mixture of 1.54g (2.60 mmole) of 4 and 4.20g (3 mole equivalent per carbonyl function) of $AlCl_3$ catalyst was heated for 18h at 150°C. The resulting deep brown colored mass crushed into smaller pieces and then treated with 150m*l* of ice-water mixture. After stirred for 1h at room temperature brown colored precipitate was separated by suction filtration, washed with diluted HCl and water several times, and then boiled with 150m*l* of acetone. After the insoluble brown colored mass, which turned to black on drying, was filtered off, acetone solution was dried over $MgSO_4$ anhydride, and evaporated to dryness to give 1.37g of light brown colored residue, which was boiled with 30m*l* of benzene to remove unreacted starting material. Benzene insoluble material was treated with cold acetone to remove any colored impurities. A total of 0.901g (58.5%) of the desired product was obtained as coloreless powder. An additional 0.092g (6.3%) of product was collected from the concentration of acetone solution to bring the total yield to 0.993g (64.8%); mp 356-359°C (dec); IR(KBr) 3200 cm^{-1} (OH stretching), 1665 (C=O stretching); ^{1}H-nmr ($CDCl_3$) δ 10.3 (s, 4, OH), 7.82 (s, 8, ArH), 4.00 (br, 8, CH_2), 2.50 (s, 12, CH_3).

5,11,17,23-Tetrakis(1-hydroxyethyl)-25,26,27,28-tetra-hydroxycalix[4]arene 7. A solution of 0.32g (0.54 mmole) of 6 in 30 m*l* of dry THF was treated with 0.06g of $LiAlH_4$, and the mixture was stirred for 6h at room temperature. The resulting suspension was treated with 70m*l* of ice-cold water then stirred for 30 min. After THF solvent was removed by evaporation the aqueous suspension was acidified by adding diluted HCl. The resulting precipitate was collected by filtration, washed with water and then dried. The slightly grey colored residue was dissolved in 30m*l* of boiling THF. After removal of THF insoluble material by filtration, THF was evaporated to dryness. The resulting residue was triturated with acetone to give 0.204g (63%) of white precipitate. Mother liquid was treated with hexane to give 0.026g (8.0%) of white powder. The total yield was 71%; mp 340-342°C (dec); IR(KBr) 3350 and 3200 cm^{-1} (OH stretchings); ^{1}H-nmr (acetone d_6) δ 7.33 (s, 8, ArH), 4.73 (q, 4, CH), 4.02 (br, 8, CH_2), 2.95 (br, 8, OH), 1.35 (d, 12, CH_3).

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References

1. C.D. Gutsche, M. Igbal, D. Stewart, *J. Org. Chem.*, **51**, 742

(1986).
2. K.H. No, Y.J. Noh, *Bull. Korea Chem. Soc.*, **7**, 314 (1986)
3. C.D. Gutsche, J.A. Levine, *J. Am. Chem. Soc.*, **104**, 2652 (1982).
4. S. Shinkai, S. Mori, T. Tsubaki, T. Sone, O. Manabe, *Tetrahedron Lett.*, **25**, 5315 (1985).
5. C.D. Gutsche, P.F. Pagoria, *J. Org. Chem.*, **50**, 5795 (1985).
6. C.D. Gutsche, L-g, Lin, *Tetrahedron*, **42**, 1633 (1986).
7. (a) K. Fries, G. Finck, *Ber.*, **41**, 4271 (1908), (b) A.H. Blatt, *Org. React.*, **1**, 342 (1942).
8. C.D. Gutsche, B. Dhawan, J.A. Levine, K.H. No and L.J. Bauer, *Tetrahedron*, **39**, 409 (1983).
9. C.D. Gutsche, B. Dhawan, K.H. No, R. Muthukrishnan, *J. Am. Chem. Soc.*, **103**, 3782 (1981).

Total Synthesis of (R,Z)-(-)-5-Tetradecen-4-olide, the Pheromone of the Japanese Beetle and Its Biological Activity Test

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Optically active (R,Z)-(-)-5-tetradecen-4-olide, the pheromone of *Popillia japonica* Newman was synthesized from (R)-2,3-O-isopropylideneglyceraldehyde as starting material. The biological activity test of the synthetic pheromone as attractant for the male Japanese beetle was tested in Korea.

Introduction

The Japanese beetle (*Popillia japonica* Newman) is a notorious pest of a variety of trees, ornamentals, and cultivated crops, and the larvae attack the roots of grasses in U.S.A.. In 1977, its pheromone was shown to be (R,Z)-(-)-5-tetradecen-4-olide(**1**) (Figure 1) by Tumlinson *et al.*[1] Male response was strongly inhibited by small amounts of its (S,Z)-isomer.[1]

Indeed, (R,Z)-**1** of 90% optical purity was less than 1/3 as active as the pure pheromone. This fact demands a highly efficient chiral synthesis of (R,Z)-**1**. The original synthesis of Tumlinson *et al.*[1] involved R(-)-glutamic acid, an unnatural aminoacid as the starting material. Since then, a number of asymmetric synthesis have been reported by resolution[2,3] and by asymmetric reduction[4-6] of an intermediate, an acetylenic keto ester, with varying degree of success. Mori's synthesis[2] depended on the optical resolution of an intermediate and resulted in the synthesis of **1** with 90% optical purity. Pirkle's resolution[3] of his intermediate by HPLC separation was more efficient and yielded 100% optically pure **1**. Three groups[4-6] have reported the asymmetric synthesis of (R,Z)-**1**. The key-step of all of the existing asymmetric syntheses was the reduction of an acetylenic keto ester with a chiral reducing agent[4-6] or with LAH plus a chiral auxiliary.[6] Noyori *et al.*[4] used a binaphthol-modified complex aluminum hydride for the reducing B-3-pinanyl-9-borobicyclo[3.3.1]-nonane, Midland *et al.*[5] (R,Z)-**1** in 100% optically pure form, by reduction of acetylenic ketone using LAH and Darvon alcohol or Chirald as a chiral auxiliary and followed by recrystallization. The syntheses via the intermediate by reducing agent were inadequate for a large scale preparation. Noyori *et al.*[4] reported the occurrence of some racemization to introduce double bond at C-6 position by the catalytic hydrogenation of the acetylenic ester.

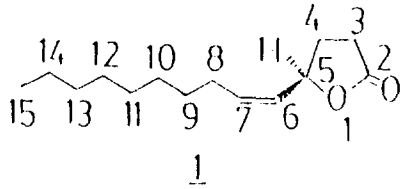

Figure 1

scale preparation. Noyori *et al.*[4] reported the occurrence of some racemization to introduce double bond at C-6 position by the catalytic hydrogenation of the acetylenic ester.

Since the pheromone can be used to survey and control this major pest, effective methods for its synthesis would be useful. Here, we wish to report a synthesis of (R,Z)-**1** using (R)-2,3-O-isopropylideneglyceraldehyde(**5**)[7] as starting material.

Results and Discussion

It has been well established that the Wittig olefination reaction when carried out between primary aliphatic aldehyde **3** and saturated aliphatic nonstabilized triphenylphosphonium ylide **2** in a "salt-free" nonpolar condition or in a dipolar aprotic solvent gives (Z)-alkene stereoselectively.[8] A simple retrosynthetic analysis (Scheme 1) reveals that the aldehyde, 5-aldehydo-2-oxotetrahydrofuran(**3**),[9] the oxidized compound